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| EXAMINER | |
|---|---|
| LUM, LEON YUN BON | |

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|---|---|
| 1641 | |

DATE MAILED: 08/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) |
|---|---|---|
| | 10/787,279 | CONNELLY ET AL. |
| | Examiner | Art Unit |
| | Leon Y. Lum | 1641 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *28 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *1-16 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-31* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20 May 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.



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## DETAILED ACTION

### *Election/Restrictions*

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claim 15, drawn to an apparatus for treating biological targets, classified in class 422, subclass 68.1.

II. Claim 16, drawn to an apparatus for treating biological targets, classified in class 435, subclass 288.2.

III. Claim 31, drawn to an implantable isolation system, classified in class 422, subclass 287.2.

IV. Claims 1-14, drawn to a process for treating biological targets, classified in class 435, subclass 286.5.

V. Claims 17-30, drawn to a process for treating biological targets, classified in class 435, subclass 7.1.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I-III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In

the instant case the different inventions have different modes of operation and different functions. Group I is an apparatus with the embodiment of a third chamber, which is not an embodiment in Groups II-III. Group II is an apparatus with the embodiment of a target specific binding agent, which is not an embodiment in Group I, and a first and second opening, which are not embodiments in Group III. Group III is an apparatus with the embodiment of first and second chambers having a maximum cross-sectional dimension of less than about 100 microns, which is not an embodiment in Groups I-II.

Therefore, Groups I-III have different modes of operation and different functions that distinguish them as unrelated inventions.

3. Inventions IV and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation and different functions. Group IV is a process that includes the step of marginating a first and second biological target, which are not steps in Group V. Group V is a process that includes the step of modifying the flow dynamics of a fluid by allowing target specific binding agent to bind with a biological target, which is not a step in Group IV.

Therefore, Groups IV-V have different modes of operation and functions that distinguish them as unrelated inventions.

4. Inventions I and IV are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case the apparatus as claimed can be used to practice the materially different process of Group V.

This relationship also applies to Groups II-III and IV.

5. Inventions I and V are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case the apparatus as claimed can be used to practice the materially different process of Group IV.

This relationship also applies to Groups II-III and V.

6. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

In addition, because these inventions are distinct for the reasons given above and the search required for each of Groups I-V is not required for the other Groups, restriction for examination purposes as indicated is proper. Groups IV-V require

searching for process methods that do not necessarily require the same search terms as Groups I-III since a reference that discloses an apparatus may not disclose method steps of using that apparatus. In addition, the reasons of distinctiveness between the groups above highlight the differences in search terms required between each of Groups I-III and Groups IV-V.

7. During a telephone conversation with Peter Mikesell on 12 July 2005 a provisional election was made with traverse to prosecute the invention of Group V, claims 17-30. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-16 and 31 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

9. The preliminary amendment filed 28 June 2004 is acknowledged and has been entered.

***Specification***

10. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claim 27 recites that "said third chamber is not concentric with said first chamber and said third chamber is disposed within said second chamber".

***Claim Rejections - 35 USC § 112***

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 20-21 and 27-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claims 20-21 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are:

With respect to claim 20, the instant claim is incomplete because it fails to recite steps on how a morphological characteristic of said biological target is modified in order to differentiate the biological target. The missing step is essential since it establishes

how and when the differentiation takes place. For example, is the biological target differentiated within the first chamber, within the second chamber, or within another chamber? Is the biological target differentiated before being captured at the capture zone or afterwards?

With respect to claim 21, the instant claim is incomplete because it fails to recite steps on how a morphological characteristic of said biological target is modified in order to devitalize the biological target. The missing step is essential since it establishes how and when the devitalization takes place. For example, is the biological target differentiated within the first chamber, within the second chamber, or within another chamber? Is the biological target differentiated before being captured at the capture zone or afterwards?

14. Claim 27 is vague and indefinite because it is unclear how the third chamber is disposed relative to the first chamber. The specification and figures disclose a series of three concentric chambers (page 22, line 15 to page 23, line 2; and Figure 8) with binding members therein, which would represent a series of first, second, and third chambers. In addition, the specification discloses a preferred embodiment wherein the first and second chambers are disclosed within a third chamber (page 31, line 23 to page 32, line 17), but does not describe how the chambers are oriented relative to each other. Therefore, since neither the specification nor the figures disclose a third chamber that is not concentric to the first chamber and simultaneously disposed in a second

chamber, as recited in the instant claims, it is unclear as to how the claimed first and third chambers are oriented relative to each other.

***Claim Rejections - 35 USC § 102***

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 17, 24-27, and 29-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Guirguis (US 5,133,363).

Guirguis reference teaches that the shuttle resin/sample container 70 (i.e. assembly) is placed within sample collection apparatus 20 (i.e. second chamber), wherein the shuttle container comprises multiple, concentric, cylindrical chambers 77, 81,85, and 87, each filled with a predetermined sequence of beads that covalently bind various antigens and antibodies, wherein chamber 77 is a control with unbound beads, chamber 81 (i.e. third chamber disposed within first and second chamber; inner wall comprised to a target specific binding agent) has beads with either antigen A and anti-B antibody thereon, and chamber 85 (i.e. first chamber disposed within second chamber) has beads with either anti-B antibody or anti-A antibody thereon. See column 3, lines 13-16; column 4, lines 29-59; and Figures 1, 3, and 5-6. In addition, Guirguis teaches

the step of pushing down the shuttle container such that a specimen sample fluid within the sample collection apparatus flows into the shuttle container and contacts the beads with ligands immobilized thereon (i.e. feeding a fluid into an assembly; inner wall is permeable to biological target) and captures through-antigen-antibody reaction the specific component of the fluid which is to be tested (i.e. allowing said target specific binding agent to bind with said biological target), wherein labeled primary antibodies are added to the sample fluid previous to the step of pushing down the shuttle container in order to for labeled antibody-antigen complexes. See column 5, lines 58-63 and column 6, lines 5-18; and Figures 7-8. Furthermore, Guirguis teaches that the upper surface of disc membrane 100 on top of the shuttle container provides a surface upon which primary antibody and/or antigen-antibody complexes are captured by secondary antibody immobilized on the membrane after flowing through the membrane from within the shuttle container (i.e. causing said biological target to migrate into a capture zone disposed within said second chamber). See column 6, lines 30-35.

With regards to claim 27, Guirguis teaches transporter assembly 50 (i.e. third chamber not concentric with said first chamber and third chamber is disposed in second chamber), wherein the transporter assembly has a hollow cylindrical piston body 52 with interior chamber 53 that collects fluid when the shuttle container is pushed down. See column 3, line 59 to column 4, line 5; column 6, lines 44-47; and Figure 3.

***Claim Rejections - 35 USC § 103***

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

19. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claims 18-19 and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guirguis (US 5,133,363) in view of Civin (US 4,714,680), and in light of Eppich et al (Nature Biotechnology, 2000).

Guirgius reference has been disclosed above, but fails to teach that said biological target comprises a stem cell.

Civin reference teaches the step isolating hematopoietic stem cells by flowing blood through membranes having antibodies specific for the stem cells immobilized therein, in order to isolate the stem cells for therapeutic applications including bone marrow transplantation. See column 3, lines 11-19; and column 7, lines 9-14 and 45-52.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Guirguis with the step isolating hematopoietic stem cells by flowing blood through membranes having antibodies specific for the stem cells immobilized therein, as taught by Civin, in order to isolate the stem cells for therapeutic applications including bone marrow transplantation. In teaching the method of isolating hematopoietic stem cells, Civin teaches the advantage of collecting blood stem cells for transplant into patients lacking stem cells, and provides motivation in collecting the stem cells using the method of Guirguis. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the step of isolating blood stem cells, as taught by Civin, in the method of Guirguis, since Guirguis teaches the flow of biological sample through membranes, and the stem cells of Civin can also flow through membranes.

With regards to claim 22, since Civin teaches isolating stem cells for transplantation, the cells would have to be removed from the solid phase membrane.

With regards to claim 23, since hematopoietic stem cells are larger than 1 micron, the membrane pore size is required to be greater than 1 micron. See page 885, right column, last paragraph of Eppich et al.

21. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Guirguis (US 5,133,363) in view of Civin (US 4,714,680), and in light of Eppich et al (Nature Biotechnology, 2000) as applied to claims 17 and 19 above, and further in view of Roberts (US 5,686,281).

Guirguis and Civin references have been disclosed above, but fail to teach that a morphological characteristic of said biological target is modified in such a way so as to differentiate said biological target.

Roberts reference teaches the introduction of chimeric constructs into hematopoietic stem cells, in order to permit the induction of effector functions such as differentiation to various cell types to provide a source of effector cells to fight virally infected diseases. See column 15, line 64 to column 16, line 27.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Guirguis and Civin with the introduction of chimeric constructs into hematopoietic stem cells, as taught by Roberts, in order to permit the induction of effector functions such as differentiation to various cell types to provide a source of effector cells to fight virally infected diseases. The differentiation step taught

by Roberts teaches the advantage of providing cells differentiated from stem cells to fight diseases, and provides motivation for differentiating the stem cells obtained by the method of Guirguis and Civin. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the differentiation step of Roberts in the method of Guirguis and Civin, since Guirgis and Civin teach the isolation of hematopoietic stem cells for therapeutic applications, and the differentiated cells of Roberts are derived from hematopoietic stem cells for the purpose of therapeutic applications.

22. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Guirguis (US 5,133,363) in view of Daluge (US 5,399,580).

Guirguis reference has been disclosed above, but fails to teach that a morphological characteristic of said biological target is modified in such a way so as to devitalize the biological target.

Daluge reference teaches denaturing virus particles, in order to release HBV DNA strands for amplification and detection using polymerase chain reaction and a hybrid-capture assay, wherein the virus particles are captured by surface-coated antibodies. See column 13, lines 36-48.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Guirguis with the step of denaturing virus particles, as taught by Daluge, in order to release HBV DNA strands for amplification and detection using polymerase chain reaction and a hybrid-capture assay. The denaturing step of

Daluge teaches the advantage of releasing DNA strands for PCR, and provides the motivation for performing the denaturing step on viral antigens obtained by the method of Guirguis. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a denaturing step, as taught by Daluge, in the method of Guirguis, since Guirguis teach the capture of antigen by antibodies, and the virus particles of Daluge are also able to be captured by antibodies.

23. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Guirguis (US 5,133,363) in view of Kaiser et al (WO 00/68689).

Guirguis reference has been disclosed above, but fails to teach that said third chamber has an inner wall comprised of a target specific binding agent.

Kaiser et al reference teaches multiple zones (i.e. chambers) in sequence, wherein each zone comprises a separate binding molecule, in order to perform cellular enrichment or purification of a particular subset of cells. See page 12, line 33 to page 13, line 1; and page 13, line 35 to page 14, line 10.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Guirguis with multiple zones (i.e. chambers) in sequence, wherein each zone comprises a separate binding molecule, as taught by Kaiser et al, in order to perform cellular enrichment or purification of a particular subset of cells. The sequential placement of chambers, as taught by Kaiser et al, teaches the advantage of sequential purification or cellular enrichment, which is the motivation for enriching cells using the apparatus taught in the method of Guirguis. In addition, one of

ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including multiple zones in sequence, as taught by Kaiser et al, in the method of Guirguis, since Guirguis teach the capture of antigen using antibodies in chambers, and the multiple zones of Kaiser et al are chambers that include capture agents.

***Conclusion***

24. No claims are allowed.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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